

Resolving the 3D Landscape of Transcription-Linked Mammalian Chromatin Folding.

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Public Summary:

Whereas folding of genomes at the large scale of epigenomic compartments and topologically associating domains (TADs) is now relatively well understood, how chromatin is folded at finer scales remains largely unexplored in mammals. Here, we overcome some limitations of conventional 3C-based methods by using high-resolution Micro-C to probe links between 3D genome organization and transcriptional regulation in mouse stem cells. Combinatorial binding of transcription factors, cofactors, and chromatin modifiers spatially segregates TAD regions into various finer-scale structures with distinct regulatory features including stripes, dots, and domains linking promoters-to-promoters (P-P) or enhancers-to-promoters (E-P) and bundle contacts between Polycomb regions. E-P stripes extending from the edge of domains predominantly link co-expressed loci, often in the absence of CTCF and cohesin occupancy. Acute inhibition of transcription disrupts these gene-related folding features without altering higher-order chromatin structures. Our study uncovers previously obscured finer-scale genome organization, establishing functional links between chromatin folding and gene regulation.

Scientific Abstract:

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